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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/112,041	07/08/98	GHETIE M	UTSD:521/WIM

HM22/1012

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EXAMINER	
HUNT, J	
ART UNIT	**PAPER NUMBER**
1642	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/112,041	Applicant(s) Ghetie et al.
	Examiner Jennifer Nichols, Nee Hunt	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Jul 18, 2000*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-9, 11-23, and 25-51* is/are pending in the application.

Of the above, claim(s) *26-42* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9, 11-23, 25, and 43-51* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Amendment

Aknowledgement is made of applicant's cancellation of claims 10, 24 and 52, in paper number 14. Applicant states in their response that non-elected claims 26-42 have been canceled, but no such amendment is of record in the case. Therefor claims 1-9, 11-23, and 25-51 are pending in the application. Claims 26-42 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-9, 11-23, 25, and 43-51 are under consideration.

Priority

1. Aknowledgement is made of applicant's amendment to the specification, claiming priority to provisional application, and substitute declaration.

Claim Rejections Withdrawn

2. All rejections of claims 10, 24, and 52 are withdrawn in light of the cancellation thereof.

3. The rejection of claims 3-7, 13-21, 45, and 48-49 under 35 U.S.C. for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention are withdrawn in light of the amendments thereto and clarifications of the record.

4. The grounds of rejection of claims 1-6 under 35 U.S.C. 102(b) as being anticipated by *Hudson, Bio/technology*, is withdrawn in light of applicant's clarification of the publication date of *Hudson*.

5. The grounds of rejection of claims 1-3, 6, 8-9, 11-15, 18-20, 22-23, 25, 43-45, 48, and 50-51 under 35 U.S.C. 102(b) as being anticipated by *Glennie, WO 91/034493*, is withdrawn in light of applicant's amendments thereto.

6. The grounds of rejection of claims 1-3 and 6 under 35 U.S.C. 102(b) as being anticipated by *Ghetie et al., Biologicals and Immunologicals*, is withdrawn in light of applicant's amendments thereto.

7. The grounds of rejection of claims 1-3 and 6 under 35 U.S.C. 102(b) as being anticipated by *Bosslet et al., US Patent 5,591,828*, is withdrawn in light of applicant's amendments thereto.

8. The grounds of rejection of claims 1, 3, 9, 11, 13, and 23 under 35 U.S.C. 102(b) as being anticipated by *Bagshawe et al., US Patent 5,683,694*, is withdrawn in light of applicant's amendments thereto.

9. All rejections of claims 1-9, 11-23, 25, and 43-51 under 35 U.S.C. 103(a) are withdrawn in light of applicant's amendments thereto.

Claim Rejections Maintained

10. The grounds of rejection of claims 1-6, 11-20, 25, 43-48, and 52 under 35 U.S.C. 102(b) as being anticipated by *Ahlem et al., US Patent 5,273,743, December 28, 1993* is maintained for reasons of record, and newly applied to amended claims 7, 21, and 49.

Applicant argues that the conjugates taught by Ahlem et al. are heteroconjugates, and that Ahlem fails to teach anything about homoconjugates, including the specific homoconjugates and homodimers instantly claimed. Applicant next argues that in Ahlem et al., none of the antibodies

have an Fc region, and applicant further asserts that claims 1, 3-6, 11, 13-20, 25, 43, and 45-48 recite that at least one monoclonal antibody does comprise an Fc region. Applicant's arguments filed 7-18-2000 have been fully considered but they are not persuasive.

With regard to applicant's arguments that Alhem et al. fails to teach homoconjugates, as set forth in the previous office action, Alhem does teach homoconjugates, for example in the abstract, column 2, lines 29-58, column 6, lines 45-48, column 9, lines 22-27, and column 13, lines 65-68, where it specifically teaches that the Fab's can have the same specificity.

With regard to applicant's argument that Alhem fails to teach a complex which comprises at least one monoclonal antibody which does comprise an Fc region, this argument is not commensurate in scope with the instant claims, which do not recite the limitation that at least one antibody of the complex comprise an Fc region.

11. The grounds of rejection of claims 1-2, 6, 11-12, and 23 under 35 U.S.C. 102(b) as being anticipated by *Cumber et al., The Journal of Immunology* is maintained for reasons of record, and newly applied to amended claims 7, 21, and 49.

Applicant argues that the conjugates taught by Cumber et al. are heteroconjugates, and that Cumber fails to teach anything about homoconjugates, including the specific homoconjugates and homodimers instantly claimed. Applicant next argues that in Cumber et al., none of the antibodies have an Fc region, and applicant further asserts that claims 1-2, 6, 11-12,

and 23 recite that at least one monoclonal antibody does comprise an Fc region. Applicant's arguments filed 7-18-2000 have been fully considered but they are not persuasive.

With regard to applicant's arguments that Cumber et al. fails to teach homoconjugates, as set forth in the previous office action, Cumber does teach homoconjugates, for example on page 120, column 2, paragraph 3, where it specifically teaches that the Fab's can have the same specificity.

With regard to applicant's argument that Cumber fails to teach a complex which comprises at least one monoclonal antibody which does comprise an Fc region, this argument is not commensurate in scope with the instant claims, which do not recite the limitation that at least one antibody of the complex comprise an Fc region.

New Grounds of Rejection

12. Claims 1, 3, 9, 11, 13, and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by *Bagshawe et al., US Patent 5,683,694, November 4, 1997.*

Bagshawe et al. teaches a conjugate comprising a monoclonal antibody that does not comprise an Fc region. The conjugate exhibits antineoplastic activity. (Column 1, lines 14-20, and column 2, lines 24-40) Bagshawe also teaches how to make the aforementioned conjugate using a mammalian monoclonal antibody (column 7- 8).

Applicant argues with regard to Bagshawe et al. that the instant reference is not prior art due to the amended priority claim in the instant application, however the effective filing date of Bagshawe et al. is prior to the instant effective filing and therefore Bagshawe et al. is prior art.

13. Claims 1-3, 6-15, 18-25, 43-45, and 48-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Glennie, WO 91/03493, March 21, 1991, Ghetie et al., Exp. Opin. Invest. Drugs, Vol 5, No 3, pages 309-321, or Bosslet et al., US Patent 5,591,828, January 7, 1997* in view of Wolff et al., WO 92/04053.

Glennie, Ghetie, and Bosslet et al. teach as applied to claims 1-3, 6, 8-15, 18-20, 22-25, 43-45, and 48, and 50-51 in the previous office action, and are newly applied to amended claims 7, 21, and 49, and reiterated below for clarity.

Glennie teaches a conjugate of two, three, or more monoclonal antibodies wherein none of the monoclonal antibodies comprise an Fc region. Glennie also teaches the said conjugate which comprises an antibody which asserts anti-neoplastic activity in conjugated form. Glennie also teaches the said conjugate which comprises an antibody which does not assert anti-neoplastic activity in unconjugated form (abstract and page 1-page 3). The conjugate comprises a monoclonal antibody which is a mammalian IgG monomer (page 7, last paragraph).

Glennie also teaches a method of making any of the aforementioned conjugates, as well as conjugates in which the first and second antibodies assert anti-neoplastic activity in conjugated

form. Glennie also teaches method of making conjugates in which none of the antibodies assert anti-neoplastic activity in an unconjugated form.(page 3, line 28-page 5, and page 8-9)

Glennie also teaches a pharmaceutical composition comprising a conjugate comprising a monoclonal antibody and a pharmaceutically acceptable carrier, wherein no monoclonal antibody comprises an Fc region. The monoclonal antibody asserts anti-neoplastic activity in conjugated form. Glennie also teaches the said conjugate which comprises an antibody which does not assert anti-neoplastic activity in unconjugated form. The conjugate comprises a monoclonal antibody which is a mammalian IgG monomer (page 19-23)

Ghetie et al. teaches a conjugate of two, three, or more monoclonal antibodies wherein none of the monoclonal antibodies comprise an Fc region. Ghetie et al. also teaches the said conjugate which comprises an antibody which asserts anti-neoplastic activity in conjugated form. Ghetie et al. also teaches the said conjugate which comprises an antibody which does not assert anti-neoplastic activity in unconjugated form (page 314, last paragraph- 315, 1st paragraph)

Bosslet et al. teaches a conjugate of two, three, or more monoclonal antibodies wherein none of the monoclonal antibodies comprise an Fc region. Bosslet et al. also teaches the said conjugate which comprises an antibody which asserts anti-neoplastic activity in conjugated form. Bosslet et al. also teaches the said conjugate which comprises an antibody which does not assert anti-neoplastic activity in unconjugated form. (Figure 1-4 and column 1, lines 12-16 and column 2, lines 7-32)

Glennie, Ghetie, and Bosslet et al. fail to teach that the immunoconjugate is a homoconjugate or homodimer.

Wolff et al. teaches antibody conjugates which are homoconjugates including dimers and multimers and that said conjugates are desirable because the produce an enhanced immune response. Wolff also provides guidance to alter or remove the Fc region of some or all of said antibody conjugates. (see for example abstract, page 3, line 25-page 4, line 20, or page 6, line 26-page 9, line 40)

Therefor it would have been *prima facie* obvious to one of ordinary skill in the art to modify the basic conjugate design of Glennie, Ghetie, or Bosslet et al. to make homoconjugates or homodimers, and one would have been motivated to make this obvious variation because homodimeric/conjugated antibody compounds produce an enhanced immune response, as taught by Wolff et al.

Applicant argues that in Glennie, Ghetie, or Bosslet et al., none of the antibodies have an Fc region and applicant further asserts that the instant claims recite that at least one monoclonal antibody does comprise an Fc region. Applicant's arguments filed 7-18-2000 have been fully considered but they are not persuasive.

With regard to applicant's argument that Glennie, Ghetie, or Bosslet et al. fails to teach a complex which comprises at least one monoclonal antibody which does comprise an Fc region, this argument is not commensurate in scope with the instant claims, which do not recite the limitation that at least one antibody of the complex comprise an Fc region.

With regard to the combination of the instant references, it is noted that it is not necessary that the claimed invention be expressly suggested by in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to one of ordinary skill in the art. (*In re Keller*, 642 F.2d 413,288 USPQ 871 9ccpa 1981)

Thus since Wolff clearly establishes the art known fact that homoconjugates are useful and desirably for certain immunotherapies, the production of a homoconjugate for m of the conjugates of the applied references would be an obvious variation.

No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Nichols, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Nichols, Nee Hunt

October 10, 2000

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